

**Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application.

**Listing of the Claims:**

Claim 1 (currently amended): A method for determining whether a test human subject has at least one auto-immune disease comprising

- a) obtaining blood from the predetermined test human subject thus obtaining a test sample;
- b) obtaining blood from a non-autoimmune human subject thus obtaining a control sample;
- c) contacting the test sample and the control sample with a combination of at least one detectably-labeled anti-CD4 antibody and at least one detectably-labeled anti-CD40 antibody;
- d) detecting the level of  $CD4^{lo} CD40^{hi}$  T cells in the test sample and in the control sample;

wherein when there is an increase in the level of  $CD4^{lo} CD40^{hi}$  T cells in the test sample as compared to the level of  $CD4^{lo} CD40^{hi}$  T cells in the control sample, the test human subject has at least one auto-immune disease.

Claim 2 (original): The method of claim 1 further comprising isolating the test sample  $CD4^{lo} CD40^{hi}$  T cells and the control sample  $CD4^{lo} CD40^{hi}$  T cells from part 1d) and determining the presence or absence of an increase in production of at least one cytokine in the test T cell population as compared to the sample T cell population.

Claim 3 (previously presented): The method of claim 2 wherein said cytokine is at least one cytokine selected from the group consisting of IL-2 (interleukin-2), IL-4 (interleukin-4), IL-6 (interleukin-6), IL-10 (interleukin-10), TGF $\beta$  (transforming growth factor  $\beta$ ) and IFN $\gamma$  (interferon- $\gamma$ ).

Claim 4 (original): The method of claim 1, wherein the auto-immune disease is selected from the group consisting of type 1 diabetes, rheumatoid arthritis, lupus, multiple sclerosis, atherosclerosis, Crohn's colitis, ulcerative gastritis, primary biliary cirrhosis, chronic obstructive pulmonary disease (COPD) and scleroderma.

Claim 5 (original): The method of claim 4, wherein the auto-immune disease is type 1 diabetes.

Claim 6 (original): The method of claim 4, wherein the COPD disease is emphysema.

Claim 7 (original): The method of claim 1, wherein said detecting is by flow cytometry.

Claim 8 (canceled)

Claim 9 (withdrawn): A method for determining whether a predetermined test subject is susceptible to developing at least one predetermined auto-immune disease comprising

- a) obtaining a first sample of blood from said predetermined test subject;
- b) obtaining a second sample of blood from said same subject;
- c) detecting the CD4<sup>lo</sup> CD40<sup>hi</sup> T cell population in said first and second samples;
- d) contacting said second test sample with at least one predetermined antigen

indicative of at least one predetermined auto-immune disease for a length of time and in an amount sufficient to obtain a positive or negative cellular response in the CD4<sup>lo</sup> CD40<sup>hi</sup> T cell population of said second sample,

- e) determining whether a positive or negative cellular response occurs in the CD4<sup>lo</sup> CD40<sup>hi</sup> T cell population of said first and said second samples by measuring at least one response selected from the group consisting of CD4<sup>lo</sup> CD40<sup>hi</sup> T cell proliferation, CD4<sup>lo</sup> CD40<sup>hi</sup> T cell death and CD4<sup>lo</sup> CD40<sup>hi</sup> cytokine production,

wherein when a positive response occurs in the CD4<sup>lo</sup> CD40<sup>hi</sup> T cell population of the second sample as compared to the response from the CD4<sup>lo</sup> CD40<sup>hi</sup> T cell population of the first sample, the predetermined subject is susceptible to developing the at least one predetermined

autoimmune disease.

Claim 10 (withdrawn): The method of claim 9, wherein a positive response is an increase in CD4<sup>lo</sup> CD40<sup>hi</sup> T cell proliferation, an increase in CD4<sup>lo</sup> CD40<sup>hi</sup> T cell death and an increase in production of at least one cytokine produced by said CD4<sup>lo</sup> CD40<sup>hi</sup> T cell population.

Claim 11 (withdrawn): The method of claim 10 wherein said at least one cytokine is selected from the group consisting of IL-2, IL-4, IL-6, IL-10, TGF $\beta$  and IFN $\gamma$ .

Claim 12 (withdrawn): The method of claim 9 wherein said at least one preselected autoimmune disease is type 1 diabetes and said antigen is pancreatic tissue.

Claim 13 (withdrawn): The method of claim 9 wherein said at least one preselected auto-immune disease is rheumatoid arthritis and said antigen is synovial tissue.

Claim 14 (withdrawn): The method of claim 9, wherein said at least one preselected auto-immune disease is multiple sclerosis and said antigen is nervous tissue.

Claim 15 (withdrawn): The method of claim 9, wherein said at least one preselected auto-immune disease is scleroderma and said antigen is skin tissue.

Claim 16 (withdrawn): The method of claim 9, wherein said at least one auto-immune disease is atherosclerosis and said antigen is cardiac tissue.

Claim 17 (withdrawn): The method of claim 9, wherein said subject is human.

Claim 18 (withdrawn): A method of modulating the proliferation of CD4<sup>lo</sup> CD40<sup>hi</sup> T cells in a subject in need of said modulation comprising at least one method selected from the group consisting of

- a) contacting said subject with at least one agent which inhibits the activation of

RAG recombinase activity;

- b) contacting said subject with an antibody molecule, or fragment thereof, to CD40;
- c) contacting said subject with an antibody molecule, or fragment thereof, to CD154;
- d) contacting said subject with at least one blocking peptide to prevent interaction of the CD40 receptor with the CD154 ligand;
- e) contacting said subject with at least one RNA molecule specifically hybridizing to the RAG2 gene product; and,
- f) contacting said subject with at least one RNA molecule specifically hybridizing to the RAG1 gene product;

wherein said contacting is for a length of time sufficient and in an amount sufficient to modulate the proliferation of CD4<sup>lo</sup> CD40<sup>hi</sup> T cells in said subject.

Claim 19 (withdrawn): The method of claim 18, part a), wherein said at least one agent is a chaetochromin or a derivative thereof.

Claim 20 (withdrawn): The method of claim 18, part b), wherein said antibody fragment is an Fab portion.

Claim 21 (withdrawn): The method of claim 18, part c), wherein said antibody fragment is an Fab portion.

Claim 22 (withdrawn): The method of claim 18, part d), wherein said blocking peptide is selected from the group consisting of SSKTTSVLQWAEKGYYTMSNNLVT (SEQ ID NO: 7) and QIAAHVISEASSK (SEQ ID NO: 8).

Claim 23 (withdrawn): The method of claim 18, part e), wherein said RNA molecule is selected from the group consisting of  
5'-AUGUCUCUGCAGAUGGUACdAdG-3' (SEQ ID NO: 9);  
5'-CUGUUACCAUCUGCAGAGACdAdU-3' (SEQ ID NO: 10);  
5'-GGUAGGAGAUCUUCUGAAGdCdC-3' (SEQ ID NO: 11);

5'-GGGGAUGGGCACUGGGUCCAUGdCdU-3' (SEQ ID NO: 12);  
5'-AGCAUGGACCCAGUGCCCAUCCdCdC-3' (SEQ ID NO: 13); and,  
5'-CUGUUACCAUCUGCAGAGACdAdU-3' (SEQ ID NO: 14).

Claim 24 (withdrawn): The method of claim 18, part f), wherein said RNA molecule is selected from the group consisting of

5'-AUGGCAGCCUCUUUCCACCCAdCdC-3' (SEQ ID NO: 15);  
5'-GGUGGGUGGGAAAGAGGGCUGCCdAdU-3' (SEQ ID NO: 16);  
5'-AAACUUGCAGCUCAGCAAAAAACdTdC-3' (SEQ ID NO: 17);  
5'-GAGUUUUUUGCUGAGCUGCAAGUdUdU-3' (SEQ ID NO: 18);  
5'-GAGUUUUUUGCUGAGCUGCAAGUdUdU-3' (SEQ ID NO: 19);  
5'-UCACAAAACCCUGGCCAUGUdCdC-3' (SEQ ID NO: 20); and,  
5'-GGAACAUGGCCAGGGUUUUGUdGdA-3' (SEQ ID NO: 21).

Claim 25 (withdrawn): The method of claim 18, wherein said subject has an increased level of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells as compared to the level of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells in a non-auto-immune subject and the modulation is a decrease in the level of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells.

Claim 26 (withdrawn): The method of claim 18, wherein said subject is human.

Claim 27 (currently amended): A kit for detecting ~~CD4<sup>lo</sup>CD40<sup>hi</sup> T cells autoimmune disease in a human subject~~ comprising

- a) at least one detectably labeled anti-CD4 antibody and at least one detectably labeled anti-CD40 antibody; and,
- b) at least one predetermined antigen indicative of at least one predetermined auto-immune disease.